Using Human Embryonic Stem Cells to Understand and to Develop New Therapies for Alzheimer's Disease

Grant Award Details

Using Human Embryonic Stem Cells to Understand and to Develop New Therapies for Alzheimer's Disease

Grant Type: Comprehensive Grant

Grant Number: RC1-00116

Investigator:

Name:	Lawrence Goldstein
Institution:	University of California, San Diego
Type:	PI

Disease Focus: Aging, Alzheimer's Disease, Genetic Disorder, Neurological Disorders

Human Stem Cell Use: Embryonic Stem Cell, iPS Cell

Cell Line Generation: Embryonic Stem Cell, iPS Cell

Award Value: $1,859,414

Status: Closed

Progress Reports

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: Year 4

View Report

Grant Application Details

Application Title: Using Human Embryonic Stem Cells to Understand and to Develop New Therapies for Alzheimer's Disease

Public Abstract: Alzheimer's Disease (AD) is a progressive incurable disease that robs people of their memory and ability to think and reason. It is emotionally, and sometimes financially devastating to families that must cope when a parent or spouse develops AD. Unfortunately, however, we currently lack an understanding of Alzheimer's Disease (AD) that is sufficient to drive the development of a broad range of therapeutic strategies. Compared to diseases such as cancer or heart disease, which are treated with a variety of therapies, AD lacks even one major effective therapeutic approach. A key problem is that there is a paucity of predictive therapeutic hypotheses driving the development of new therapies. Thus, there is tremendous need to better understand the cellular basis of AD so that effective drug and other therapies can be developed. Several key clues come from rare familial forms of AD (FAD), which identify genes that can cause disease when mutant and which have led to the leading hypotheses for AD development. Recent work on Drosophila and mouse models of Alzheimer's Disease (AD) has led to a new suggestion that early defects in the physical transport system that is responsible for long-distance movements of vital supplies and information in neurons causes neuronal dysfunction. The type of neuronal failure caused by failures of the transport systems is predicted to initiate an autocatalytic spiral of biochemical events terminating in the classic pathologies, i.e., plaques and tangles, and the cognitive losses characteristic of AD. The problem, however, is how to test this new model and the prevailing "amyloid cascade" model, or indeed any model of human disease developed from studies in animal models, in humans. It is well known that mouse models of AD do not fully recapitulate the human disease, perhaps in part because of human-specific differences that alter the details of the biochemistry and cell biology of human neurons. One powerful approach to this problem is to use human embryonic stem cells to generate human neuronal models of hereditary AD to test rigorously the various hypotheses. These cellular models will also become crucial reagents for finding and testing new drugs for the treatment of AD.

Statement of Benefit to California:	Alzheimer's Disease (AD) is emotionally devastating to the families it afflicts as well as causing substantial financial burdens to individuals, to families, and to society as a whole. In California, the burden of Alzheimer's Disease is substantial, so that progress in the development of therapeutics would make a significant financial impact in the state. Although there are not a great deal of data about the burden of AD in California specifically, the population of California is 12% of that of the United States and most information suggests that California has a "typical" American burden of this disease. For example, information from the Alzheimer's Association (http://www.alz.org/alzheimers_disease_alzheimer_statistics.asp) reveals: 1) An estimated 4.5 million Americans have Alzheimer's disease, which has more than doubled since 1980. This creates an estimated nationwide financial burden of direct and indirect annual costs of caring for individuals with AD of at least $100 billion. Thus, a reasonable estimate is that California has more than half a million AD patients with an estimated cost to California of $12 billion per year! 2) One in 10 individuals over 65 and nearly half of those over 85 are affected, which means that as our population ages, we will be facing a tidal wave of AD. Current estimates are that with current rates of growth that the AD patient population will double or triple in the next 4 decades. 3) The potential benefit of research such as that proposed in this grant application is that finding a treatment that could delay onset by five years could reduce the number of individuals with Alzheimer's disease by nearly 50 percent after 50 years. This would be significant since a person with Alzheimer's disease will live an average of eight years and as many as 20 years or more from the onset of symptoms. Finding better treatments will thus have significant financial benefits to California. 4) After diagnosis, people with Alzheimer's disease survive about half as long as those of similar age without AD or other dementia. 5) In terms of financial impact on California families, the statistics (http://www.alz.org/alzheimers_disease_alzheimer_statistics.asp) are that more than 7 out of 10 people with Alzheimer's disease live at home. Almost 75 percent of their care is provided by family and friends. The remainder is "paid' care costing an average of $19,000 per year. Families pay almost all of that out of pocket. The average cost for nursing home care is $42,000 per year but can exceed $70,000 per year in some areas of the country. The average lifetime cost of care for an individual with Alzheimer's is $174,000. Thus, any progress in developing better therapy for AD will have a substantial positive impact to California.